BRAZ J INFECT DIS 2017;xxx(xx):xxx–xxx

The Brazilian Journal of
INFECTIOUS DISEASES

www.elsevier.com/locate/bjid

Original article

A cross-sectional study assessing the pharyngeal carriage of *Neisseria meningitidis* in subjects aged 1–24 years in the city of Embu das Artes, São Paulo, Brazil

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ARTICLE INFO

Article history:
Received 14 December 2016
Accepted 20 June 2017
Available online xxx

Keywords:
Carriage
Meningococcal disease
Neisseria meningitidis
Pharyngeal
Serogroup

ABSTRACT

Meningococcal carriage is a prerequisite for invasive infection. This cross-sectional study assessed the pharyngeal carriage prevalence in healthy subjects aged 1–24 years in Embu das Artes city, São Paulo, Brazil. Pharyngeal swabs were examined for the presence of *Neisseria meningitidis*. The isolates were tested for different serogroups using agglutination and polymerase chain reaction. A logistic regression model assessed any independent association between *Neisseria meningitidis* carriage and various risk factors. A total of 87/967 subjects (9%, 95% Confidence Interval (CI): 7.3–11.0) tested positive for *N. meningitidis*: 6.2% (95% CI: 3.8–9.4) in 1–4 years, 8.5% (95% CI: 5.1–13.0) in 5–9 years, 12.5% (95% CI: 7.8–18.6) in 10–14 years, 12.6% (95% CI: 7.4–19.7) in 15–19 years and 9% (95% CI: 4.9–14.9) in 20–24 years age groups. Highest carriage prevalence was observed in adolescents 10–19 years old. Serogroup C was predominant (18.4%) followed by serogroup B (12.6%). The 15–19 years age group showed a significant association between number of household members and carriers of *N. meningitidis*. This cross-sectional study is the first in Brazil to evaluate meningococcal carriage prevalence and associated factors in a wide age range.

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http://dx.doi.org/10.1016/j.bjid.2017.06.005

Introduction

Meningococcal disease is a serious, rapidly developing, and potentially fatal disease affecting people worldwide with varying incidence depending on the geographical area.[1] Around 1.2 million cases of meningococcal infection occur annually with 135,000 related deaths.[2] *Neisseria meningitidis* is one of the major causes of bacterial meningitis globally.[3] Pharyngeal carriage of *N. meningitidis* has been considered to be a prerequisite for the development of invasive meningococcal disease (IMD) and known to be essential for transmission.[4] The exact mechanism by which a pharyngeal colonization changes into an invasive disease status is not entirely clear. The possible mechanisms that have been suggested are bacterial virulence factors, host susceptibility, including age, prior viral infection, and smoking may ultimately lead to invasive meningococcal disease.[5,6] *N. meningitidis* serogroups A, B, C, W, Y, and X account for the majority of IMD cases.[2] Globally, meningococcal carriage rates between 5% and 24% have been reported for children and adolescents.[7]

Meningococcal disease is endemic in Brazil and 1.5–2.0 cases per 100,000 inhabitants were reported during 2000–2009.[8] Outbreaks of IMD caused by various serogroups have been reported.[9,10] Since 2002, the proportion of cases attributed to meningococcal serogroup C has increased significantly and it is now the most frequent serogroup.[1,11,12] After this serogroup C epidemic, Brazil included the meningococcal C conjugate vaccine into the National Immunization Program in 2010.[1,12] In addition, studies describing meningococci carriage in Brazil are limited, with few specific studies in adolescents and young adults.[8,12–14] No recent data are available on carriage across different age groups from infancy to adulthood and this remains a key knowledge gap. Further data are needed to help understand both the serogroup distribution and disease transmission as they may be useful to help identifying the age groups with higher carriage prevalence rates that could be targeted for vaccination against meningococcal disease and to assess the impact of current vaccination strategies. This information is crucial to support the use of monovalent meningococcal C conjugate vaccine and to gauge if there is a need for another meningococcal vaccine in the country. In this perspective, this cross-sectional study was conducted to assess the prevalence of *N. meningitidis* carriage and associated factors in among children and adolescents aged 1–24 years.

Materials and methods

Study design and subjects

This was a cross-sectional study (GSK study identifier: 113609) conducted in one co-ordinating center, Universidade Federal de São Paulo, in partnership with the Municipal Secretariats of Health and Education in the city of Embu das Artes, São Paulo State, Brazil. Embu das Artes had a population of 240,230 in 2010, with 75% living in the suburbs, and 25% in the city center.[15] The city municipality has 14 Basic Healthcare Units (UBS). Subjects were recruited from six UBS (four in suburbs and two in city center). Also, students from primary (6–14 years) and secondary grades (15–18 years) from three schools were invited; two schools in the suburbs and 1 in the city center. Each subject received a single visit.

At the time of enrolment, subjects aged 1–24 years were stratified by age into five groups, i.e. 1–4 years, 5–9 years, 10–14 years, 15–19 years and 20–24 years. This study is part of a larger study assessing seroprevalence of hepatitis A virus (HAV), varicela-zoster virus (VZV), and meningococcal carriage. For the computation of sample size, HAV seroprevalence per age group was considered. After adjusting for 10% non-evaluable subjects, it was planned to enroll 1000 subjects (333 subjects in 1–4 years, 222 in 5–9 years, 167 in 10–14 years, 139 each in 15–19 years and 20–24 years age group) in order to have 900 evaluable subjects (300, 200, 150, 125, and 125 subjects in 1–4, 5–9, 10–14, 15–19 and 20–24 years age group, respectively). Once the target number was reached in a particular age group, enrolment was to be terminated for that age group. The study was conducted from October 2011 to May 2012.

All subjects aged 1–24 years, living in Embu das Artes, São Paulo were eligible to be enrolled in the study. The study was approved by the Ethics Committee of Universidade Federal de São Paulo/Hospital São Paulo, São Paulo, Brazil and conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from the subject/parents/legally acceptable representatives of the subject prior to the performance of any study-specific procedure. A written informed assent was obtained from subjects aged >10 years and below the legal age of consent according to local regulations.

Assessments

Recording of demographic and socioeconomic variables

The subject or parents/legally acceptable representatives of the subjects enrolled in the study were provided a questionnaire to inquiring about age, gender, area of residence, socioeconomic factors, and previous history of medical and meningococcal vaccination. The socioeconomic factors included family income (total or per capita), number of household members, attendance to an educational establishment (public or private), and type of health system used by subjects (public or private).

Laboratory assays

A pharyngeal alginate swab was collected from the posterior pharyngeal wall of each subject and placed in a tube with 1-mL Skim Milk Tryptone Glucose Glycerine (STGG) transport medium and sent to the central laboratory of Universidade Federal de São Paulo at room temperature (20–26 °C) within five hours for subsequent analysis. An aliquot of 100 μL was plated onto selective Thayer-Martin medium modified with VCNT (vancomycin, colistin, nystatin and trimethoprim). All swab specimens were tested using latex agglutination for species identification and serogroups A, B, C, W, and Y. In parallel, real-time polymerase-chain reactions (qPCR) for meningococcal identification and genogroups A, B, C, W, X

Please cite this article in press as: Weckx LY, et al. A cross-sectional study assessing the pharyngeal carriage of *Neisseria meningitidis* in subjects aged 1–24 years in the city of Embu das Artes, São Paulo, Brazil. Braz J Infect Dis. 2017. http://dx.doi.org/10.1016/j.bjid.2017.06.005